Atty. Docket No. 24222-X3

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	CHERUKURI, S. Rao	Attorney Docket:	24222-X3
Filing Date:	10/19/2001	Examiner:	Fubara, B.
Serial No.:	09/982,093	Group Art Unit:	1615
Title:	Drug Delivery Systems		

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF S. Rao CHERUKURI UNDER 37 C.F.R. § 1.132

I, S. Rao CHERUKURI, citizen of United States of America, hereby declare that:

1. I have a Bachelor of Pharmacy and a Master of Pharmacy degrees, both from Andhra University, India, and an MBA from University of Pennsylvania, Wharton School of Management. My career in the United States started in 1973 as R&D Manager with Philadelphia Chewing Gums Corporation, Haverton, PA. From 1978 to 1981, I worked as Senior Research Manager, R&D at E.R. Squibb/Life Savers Corporation. In 1981 I joined Warner Lambert & Company and was their Director of Worldwide Technology Development when I left in 1991. I joined Fuisz International, Chantilly, VA in 1992 as Senior Director of Technology and held several progressively senior research and management positions and became President, Consumer Healthcare division. I left Fuisz in 2000, and founded Capricorn Pharma Inc., in Frederick, MD to develop innovative technologies in pharmaceutical, confectionary and neutraceutical businesses. My curriculum vitae is set forth in Appendix A to this Declaration. Over the years, from 1978 till to-date, my work (as a sole inventor or as a co-inventor) resulted in issuance of about one hundred United States patents and several international counterparts. Please see

Appendix B for a list of my issued U.S. patents. In view of the above, I believe that I am one of skill in the art in the subject matter of the above-identified application.

2. I have read the subject application papers and the Office Action issued February 2, 2005. I am aware of the issues raised by the Patent Office in the previous and pending Office Actions, and in particular the reference of record, U.S. Patent 6,197,828 issued to Jerussi, et al (hereinafter, "Jerussi Patent").

3. All experiments disclosed in this Declaration were designed and supervised by me and were conducted by Mr. Revanth Babu Mutyala while acting under my constant guidance and supervision. Mr. Mutyala has been employed since June 2004 as a Pharmaceutical Scientist in the Research & Development department at Capricorn Pharma.

4. The experiments as disclosed in the present Declaration were conducted to compare the caplets of about 1mm to about 7 mm as disclosed and claimed in the above-referenced pending application with the relevant product(s) of Jerussi's Patent. The comparison would include desirable attribute, including the claimed element, namely, dissolution profile.

5. Using the Jerussi Patent as guide, I attempted to prepare oral formulations as described in Example 7, column 26, line 28 through column 27, line 22. Example 7 discloses two oral formulations, one a hard gelatin capsule dosage form and the other a compressed tablet dosage form. The hard gelatin dosage form is simply a capsule filled with blended powder of the active drug and is not expected to provide any controlled or extended release properties. Therefore, this dosage form cannot serve as a comparative product for present purposes. Accordingly, this dosage form was not prepared or used in comparing with a product of the subject invention.

6. Subsequent to the capsule formulation, Jerussi Patent disclosed a compressed tablet dosage form. There were three strengths disclosed with their composition in TABLE III. I attempted to follow the exact procedure as outlined in column 27, lines 16-20. For illustration purposes, I attempted to use the example of 100mg of the active drug, in our

case being Venlafaxine HCl. The details of this experiment are set out in the following paragraphs 7-12.

7. EXPERIMENT 1: Microcrystalline cellulose (90mg), pregelatanized starch (82.80mg) and Croscarmellose sodium (7.0mg) were mixed together in a double cone blender. The active ingredient Venlafaxine HCl (100mg) was blended with the mixture of excipients until a uniform blend was formed. The texture was a fine granular powder.

8. The dry blend was screened through an ASTM mesh#20 and was blended with magnesium stearate (0.2mg) which was previously sifted through ASTM mesh#40.

9. I attempted to compress the resulting powder blend using Pilot Tablet press with 10 Stations. This equipment is expected to produce a tablet of 9mm size. However, the powder blend was not compressible into a tablet, i.e., remained as a powder.

10. EXPERIMENT 2: In order to improve compressibility of the composition, I attempted to granulate the product, even though granulation was not suggested in the Jarussi Patent Example 7.

11. Using the procedures described above in paragraph 7, dry blended fine powder was obtained. Separately, a 5% w/v concentrated solution of Plasdone K-29/32 (Povidone) (8.40mg) was prepared in a glass beaker in isopropyl alcohol 99% USP. The dry blend was wet granulated with povidone solution.

12. The wet granulated material was dried in a Thelco lab dryer. The dried material was sifted on a ASTM mesh# 18 and was blended with magnesium stearate (0.2mg) lubricant, which was previously sifted through ASTM mesh#40.

13. I attempted to compress the material on a pilot tablet press of 10 stations and was operated at 12 rpm. This equipment is expected to produce a tablet of 9mm size. However, the powder blend was not compressible into a tablet, i.e., remained as a powder.

14. EXPERIMENT 3: In order to improve compressibility and provide hardness to the tablets to be formed, Experiment 2 above was repeated with a slight modification. The procedure described in Paragraph 11 was followed exactly as before, but in paragraph 12, the modification entailed adding talc (4.92mg) to the magnesium stearate blend.

15. I attempted to compress the material on a pilot tablet press of 10 stations and was operated at 12 rpm. This equipment is expected to produce a tablet of 9mm size. The material had satisfactory compressibility, but the tablets did not have sufficient hardness and the tablets are sticking to the punches. Therefore, this product was not of pharmaceutical quality and thus could not be used for comparative dissolution purposes.

16. EXPERIMENT 4: To improve tablet hardness and minimize or eliminate tablet stickiness, Experiment 3 was modified further. The modification entailed adding a higher amount of talc (16.43mg) to the magnesium stearate blend. With this modification, I was able to produce 9mm tablets of acceptable hardness and compressibility.

17. The product was subject to dissolution conditions. Sampling points were:- 1, 2, 4, 6, 10, 12, 18, 24 hrs. For each test, 37.5mg/75mg/150mg of venlafaxine was used. 8mL samples were withdrawn at predetermined times using an automated sampler. The venlafaxine concentration in each sample was determined using an HPLC using the method described under the Assay for all dissolution media. The percentage of venlafaxine released over time was calculated and plotted as an average of 6 runs using calibration curves consistent with Beer's law.

18. The assay conditions were as following: Column: Zorbax Eclipse XDB-C_8, 5µm, 4.6 x 150mm; Mobile phase: Aqueous 0.02M NaH_2PO_4 : H_3PO_4(ml) : Acetonitrile :1-Heptanesulfonic acid, Sodium salt (700:0.6:300:5mM); flow rate: 1.0 ml/min; column temperature: 25C; injection volume : 10 uL; UV detection: 226 nm; run time: 8 minutes. The data are presented in graphical form in Appendix C.

19. EXPERIMENT A: Venlafaxine mini-tablets were prepared by essentially following the methods disclosed in the subject application. The mini-tablets were subject to dissolution conditions. The data are presented in graphical form in Appendix C.

20. As can be seen by comparing the dissolutions in Appendix C, venlafaxine mini-tablets of the subject application having the size of 3mm have provided a controlled release of the active over a time span of about 24 hrs. In contrast, the venlafaxine tablets of 9mm size made according to the Jarussi Patent disclosure provided a quick release of the active and thus are not suitable for controlled release applications.

21. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 21st July 2005

S. Rao CHERUKURI

Appendix A

CURRICULUM VITAE OF S. Rao CHERUKURI

241 Britten Ford Dr
Vienna VA 22182

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Experience

Capricorn Pharma Inc. **4/2000 to present**
Founder, President and CEO **Frederick, MD**

Negotiated purchase of Capricorn facility from original owner, Aspen Holdings (South Africa), built management team and board, raised capital and managed all aspects of operations to date.

- Assembled management team with over 100 years of combined pharmaceutical experience and over hundred US and a multitude of international patents
- Raised debt and equity funding to meet working capital needs and fund additional capital investment in the facility
- Developed 5 products based of 16 proprietary technologies with 3 patents approved and 14 more pending
- Negotiated encapsulation supply contracts with leading European confectioners and trial plans with leading U.S. pharmaceutical firms
- Negotiated strategic partnership with a major Indian pharmaceutical firm to gain low cost access to their "specialty" generic R&D pipeline

Biovail Corporation/Fuisz Technologies Ltd. **11/92 to 3/00**
Chantilly VA 22182

President, Consumer Healthcare Division7/98 to 3/00	
Executive Vice President, Food and Nutraceutical Division	4/97 to 6/98
Sr. Vice President, Food Division	7/95 to 3/97
Vice President, OTC R&D	1/94 to 6/95
Vice President, Special Projects	4/93 to 12/93
Sr. Director, Technology Development	11/92 to 3/93

Fuisz/Biovail Experience And Accomplishments

- Developed business partnerships and launched products in more than eight countries,including USA, with licensing and supply agreements.
  - Partners include Otsuka-Pharmavite/USA, Abbott International Laboratories Columbia/Mexico, Beeline Healthcare/Ireland-UK, UK Forum, Pharma-Vicci/ Denmark, ConAgra/ USA, Dandy-Sakiz/ Turkey, CSM Leaf/Netherlands.
  - First year revenue exceeded with $5.4 million development/licensing fees and $6 million sales, with a retail value of more than $30 million.
  - Planned new products and global expansion of existing products
- Associated with development of proprietary technology platforms leading to fast melt and easy chew pharmaceutical tablets, nougat soft chew, dry beverages, oral hygiene products, herbals and medicated confectionery and chewing gums, encapsulated ingredients for products such as Tums, Xylofresh and Nicorette Gum.
- Started manufacturing operations with limited capital and used success-based investment strategy to maintain a high rate of return.

- Created new business culture, with focus on customer needs; product superiority; and speed of action
  - Customer focus: Product value proposition, therapeutic claims and cost
  - Product superiority: Quality; global thinking and planning;
  - Speed of Action: Faster to market with greater manufacturing cost effectiveness.

Warner Lambert Co. Consumer Products R&D Center **1981 to 1992**
Director, Worldwide Technology Development **Morris Plains, New Jersey**
OTC Products, Confectionery delivery systems, Encapsulations, Chewing Gum Bases, Materials research. Developed key aspects of global brands such as Listrine, Hall's, Rolaids, Trident, Dentyne, Clorets, Efferdent, and Remegel.

Squibb/ LifeSavers Division **1978 to 1981**
Sr. Research Manager – R&D **Port Chester, New York**
Developed unique dosage forms and chewing gum bases.

Philadelphia Chewing Gums Corporation **1973 to 1978**
Manager, R&D and Technical Services **Havertown, PA.**

Warner Lambert Ltd. (India) **1971 to 1972**
Production Manager- Confections **Hyderabad, India.**
Managed production of a wide range of products, including the Hall's cough drop line and assorted gums and mints

Indian Drugs and Pharmaceuticals Ltd. **1966 to 1970**
Senior Manager- Pharmaceutical Product Development **Hyderabad, India.**

EDUCATION

MBA, Wharton School, University of Pennsylvania	1978
M.S. in Pharmaceutics, Andhra University, Vizag, India	1966
B.S. in Pharmacy, Andhra University, Vizag, India	1964

PUBLICATIONS:

More than ninety U.S. Patents and more than three hundred international patents issued.

ASSOCIATIONS:

American Association of Pharmaceutical Scientists
Controlled Release Society
Product Development and Management Association
Wharton Alumni Association
American Association of Cereal Chemists
Institute of Food Technologists

PERSONAL:

Married with two daughters. U.S. Citizen. Interests include jogging and tennis.

APPENDIX B

S. Rao CHERUKURI'S U.S. PATENTS

6,589,556	Rapid-melt semi-solid compositions, methods of making same
6,555,145	Alternate encapsulation process and products produced therefrom
6,482,465	Positive hydration method of preparing confectionery and product therefrom
6,406,717	Rapid-melt semi-solid compositions, methods of making same
6,375,982	Rapid-melt semi-solid compositions, methods of making same
6,365,209	Confectionery compositions and methods of making
6,344,222	Medicated chewing gum delivery system for nicotine
6,224,939	Method and apparatus for forming an encapsulated product matrix
6,174,514	Breath Freshening chewing gum with encapsulations
6,132,797	Method of preparing mesomorphic sugar products
5,976,603	Fiber and vitamin-fortified drink composition and beverage
5,965,162	Process for forming chewable quickly dispersing multi-vitamin preparation
5,935,600	Process for forming chewable quickly dispersing comestible unit
5,895,664	Process for forming quickly dispersing comestible unit and product therefrom
5,876,506	Mesomorphic sugar and products therefrom
5,824,342	Flash flow formed solloid delivery systems
5,804,247	Positive hydration method of preparing confectionary and product therefrom
5,744,180	Comestibles containing stabilized highly odorous flavor component delivery
5,654,003	Process and apparatus for making tablets and tablets made therefrom
5,633,027	Confectioneries containing stabilized highly odorous flavor component delivery
5,587,198	Positive hydration method of preparing confectionery and product therefrom
5,587,172	Process for forming quickly dispersing comestible unit and product therefrom
5,582,855	Flash flow formed solloid delivery systems
5,556,652	Comestibles containing stabilized highly odorous flavor component delivery
5,549,917	Flash flow formed solloid delivery systems
5,503,862	Method of subjecting a protein-containing material to flash flow processing
5,456,932	Method of converting a feedstock to a shearform product and product thereof
5,284,659	Encapsulated flavor with bioadhesive character in pressed mints and confections
5,266,335	Microencapsulated flavoring agents and methods for preparing same
5,204,129	Method for preparing pulverized polydextrose which is substantially free of acids
5,110,608	Chewing gums having longer lasting sweetness
5,108,763	Microencapsulated high intensity sweetening agents having prolonged sweetness
5,106,632	Enhanced sweetness of acesulfame-K in edible compositions
5,087,460	Reduced-calorie confectionery coated chewing gum compositions
5,082,671	Low moisture sucralose sweetened chewing gum
5,080,910	Stabilized chlorodeoxysugar sweetening agents in powder form and methods
5,066,511	Method for preparing pulverized polydextrose which is substantially free of acids
5,064,658	Encapsulated synergistic sweetening agent compositions comprising aspartame
5,061,496	Stabilized chlorodeoxysugar sweetening agents in liquid medium and methods
5,059,429	Sucralose sweetened chewing gum

5,059,428	Synergistic sweetening compositions containing polydextrose chlorodeoxysurgar
5,059,416	Zinc compound delivery system with improved taste and texture
5,057,328	Food acid delivery systems containing polyvinyl acetate
5,045,326	Non-staling aerated bubble gum
5,043,169	Stabilized Sweetner Composition
5,030,459	High impact mint flavor for high base chewing gum
5,023,093	Reduced calorie chewing gum base and compositions containing the same
5,013,716	Unpleasant taste masking compositions and methods for preparing same
5,009,893	Breath-freshening edible compositions of methol and a carboxamide
5,004,595	Multiple encapsulated flavor delivery system and method of preparation
4,983,405	Reduced and low-calorie sugar and sugarless chewing gum compositions
4,983,404	Controlled release flavor system and method of preparation
4,981,698	Multiple encapsulated sweetener delivery system and method of preparation
4,980,178	Reduced calorie center-filled chewing gum compositions
4,980,177	Reduced-calorie saliva stimulating chewing gum compositions and methods
4,971,806	Multi-layered chewing gum composition having different rates of flavor release
4,971,797	Stabilized sucralose comple
4,971,787	Antacid chewing gum
4,961,935	Sugarless, substantially anhydrous chewing gum compositions and methods
4,954,353	Anhydrous chewing gum with improved stability
4,959,225	Synergistic sweetening compositions containing chlorodeoxysugars and maltitol
4,933,190	Multiple encapsulated sweetener delivery system
4,933,189	Chewing gum having longer lasting sweetness
4,933,188	Chewing gum compositions with improved physical stability
4,931,293	Food acid delivery systems containing polyvinyl acetate
4,915,958	High-base gum composition with extended flavor release
4,900,563	Fructose sweetened chewing gum compositions
4,872,884	Reduced calorie chewing gum base and compositions containing the same
4,853,212	Reduced base content chewing gum compositions having anesthetic properties
4,839,184	Stable sweetner delivery system for use with cinnamon flavors
4,832,962	Chewing gum and confectionery compositions containing a soy flavor enhancer
4,822,597	Anesthetic-containing chewing gum compositions
4,816,265	Sweetener delivery systems containing polyvinyl acetate
4,803,082	Flavor and sweetness enhancement delivery systems and method of preparation
4,794,003	Polyvinylacetate bubble gum base composition
4,765,991	Reduced calorie chewing gums and method
4,753,805	Tabletted chewing gum composition and method of preparation
4,724,151	Chewing gum compositions having prolonged breath-freshening
4,722,845	Stable cinnamon-flavored chewing gum composition
4,721,620	Polyvinylacetate bubble gum base composition
4,590,075	Elastomer encapsulation of flavors and sweeteners, long lasting flavored chewing
4,587,125	Non-staling chewing gum compositions and improved method of preparation
4,581,234	Non-staling, substantially moistureless chewing gum compositions
4,579,738	Non-staling chewing gum compositions and improved method of preparation
4,518,615	Non-adhesive chewing gum base composition
4,497,832	Chewing gum composition having enhanced flavor-sweetness

4,490,395	Chewing gum with improved stability
4,409,244	Chewing gum containing fructose syrup
4,371,549	Stable liquid red beet color and chewing gum containing same
4,352,825	Coextruded chewing gum containing a soft core portion
4,352,823	Coextruded chewing gum containing a soft non-SBR gum core portion
4,352,822	Gum base, chewing gum containing same and method
4,317,838	Method for applying sugarless coating to chewing gum and confections
4,316,915	Center-filled chewing gums
4,271,199	Sugar-containing chewing gum having smooth texture and long-lasting sweetness
4,271,198	Chewing gum having a soft texture
4,271,197	Chewing gum containing sugar substitute
4,250,195	Method for applying soft flexible sugar coating to fresh chewing gum
4,238,510	Sugarless coating for chewing gum and confections and method

APPENDIX C

COMPARISON OF DISSOLUTION

S.No.	Time (hrs)	Jerussi et al	Rx-VFC-25R5(D)
1	0	0	0
2	0.25	95.34	
3	0.5		
4	1.0		4.01
5	2.0		13.41
6	4.0		34.39
7	6.0		47.65
8	10.0		66.98
9	12.0		72.75
10	18.0		86.06
11	24.0		92.18